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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,916	03/02/2006	Biao He	UCSF-374	8961

20350 7590 08/05/2009

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
08/05/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/570,916	HE ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,12 and 26-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,12 and 26-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/9/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of claims 1-3, 12, a method for detecting lung cancer, in the reply of 5/29/09 is acknowledged.

Applicant adds new claims 26-31.

Accordingly, claims 1-3, 12, 26-31, a method for detecting lung cancer, SEQ ID NO:1, are examined in the instant application.

The embodiment of claims 1-3, 12, 26-31, as drawn to a method for detecting cancers other than lung cancer are withdrawn from consideration as being drawn to non-elected invention.

Objection

Figure 3A is objected to, because it is not readable.

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 12, 26-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting lung cancer, comprising detecting

decrease in the level of SEQ ID NO:1, or a nucleic acid encoding SEQ ID NO:2 in lung cancer tissue as compared to non-cancerous lung tissue, wherein the cancer is characterized by having methylation of the SOCS-3 promoter comprising SEQ ID NO:3, does not reasonably provide enablement for: 1) a method for detecting a cancer or lung cancer, comprising detecting decrease in the level of SEQ ID NO:1 or a nucleic acid encoding SEQ ID NO:2 in a biological sample as compared to normal, wherein the cancer is characterized by having a methylation of a SOCS-3 promoter or 2) a method of monitoring the efficacy of a therapeutic treatment of cancer, comprising measuring the level of a nucleic acid encoding SEQ ID NO:2 prior to and during therapeutic treatment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

To comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, the specification must enable one skilled in the art to make and use the claimed invention without undue experimentation. The claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The specification discloses that the level of the SOCS-3 of SEQ ID NO:1 is decreased in primary lung cancer tissue of patients having non small lung cancer (NSCLC) as compared to

matched normal counterpart (p.52-53, Example 2). The specification discloses that dense methylation of CpG islands in the SOCS-3 promoter is found in NSCLC lung cancer tissues as compared to minimal methylation of said region in normal sample (p.53, second paragraph). The specification discloses that The term "SOCS-3" refers to nucleic acid polymorphic variants, alleles, mutants, and interspecies homologues that have a nucleic acid sequence that has greater than about 90%, preferably greater than about 95%, 97%, 98%, 99%, or higher nucleotide sequence identity, preferably over a region of at least about 30, 50, 100, 200, 500, 1000, or more nucleotides, to SEQ ID NO:l (para 26 on page 7).

A biological sample encompasses any tissues to which lung cancer cells metastasized to. It is unpredictable that metastasized prostate cells still express the claimed sequences, because expression of a sequence could be lost during the progression toward metastasis. For example, Kibel, AS et al, 2000, J urol, 164(1): 192-6, teach that gene expression in the chromosomal region 12p12-13 is different in primary and metastatic prostate cancer cells, and that inactivation in the chromosome region 12p12-13 occurs prior to metastasis. Similarly, Dong et al, 2000, Cancer Research, 60: 3880-3883, teach that deletion of a region in the chromosome 13q21 is associated with aggressive prostate cancer, as compared to less aggressive prostate cancer, such as primary prostate cancers that are not yet differentiated (abstract, and figure 1 on page 3882). Russo, V et al, 1995, Int J Cancer, 64: 216-221, teach that analysis of multiple metastatic lesions and primary breast tumors show that in some cases the MAGE gene expression is lost during metastasis, but in some other cases, in metastasis nodes derived from MAGE-negative primary tumors, MAGE gene expression is detected (abstract, and table II on page 220).

Moreover, one would not know how to perform the claimed method, because it is not clear what constitutes **normal** level, which could be any arbitrary number.

Further, in view of the disclosure in the specification, **SOCS-3 promoter**, without being accompanied by a sequence identification number, as claimed in claim 1, encompasses promoter of **SOCS-3 variants**, with unknown structure and function.

Applicants have not shown how to make and use the claimed SOCS-3 variants. Protein chemistry is probably one of the most unpredictable areas of biotechnology. Such unpredictability applies as well to nucleic acids that encode proteins. Bowie (Science, 1990, 257:1306-1310) teaches that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie further teaches that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor

binding and biological activity of the protein and by Lazar et al (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein.

Moreover, one cannot predict that measuring the level of a nucleic acid encoding SEQ ID NO:2 prior to and during therapeutic treatment would effectively **monitor the efficacy of a therapeutic treatment of lung cancer**, because one cannot predict, nor there is indication that the level of SEQ ID NO:1 is effected by a therapeutic treatment, such as a chemotherapeutic drug.

MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In constrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the claimed invention, there would be an undue quantity of experimentation required for one of skill in the art to practice the claimed invention, that is commensurate in scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 26, 27, 28, 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Wikman et al, Oncogene, August 2002, 21: 5804-5813, and as evidenced by WO2004022778-A1 (Sutherland et al, published on 03/18/2004).

Claims 1, 2, 26-28, 31 are as follows:

Claim 1. (Previously Presented) A method of detecting cancer in a patient, the method comprising the steps of:

(i) determining the level of a transcript encoding SEQ ID NO:2 in a biological sample from the patient; and

(ii) detecting a decrease in the level of the transcript relative to normal, thereby detecting the presence of cancer in the patient;

wherein the cancer is characterized by having a methylation of a SOCS-3 promoter.

Claim 2. (Original) The method of claim 1, wherein the cancer is lung cancer.

Claim 26. (Previously Presented) The method of claim 1, wherein the step of determining the level of the transcript comprises a nucleic acid hybridization assay.

Claim 27. (Previously Presented) The method of claim 26, wherein the nucleic acid hybridization assay is selected from the group consisting of Northern blot, dot blotting, in situ hybridization, RNase protection, and probing a DNA microchip array.

Claim 28. (Previously Presented) The method of claim 1, wherein the transcript comprises SEQ ID NO: 1.

Claim 31. (Previously Presented) The method of claim 1, wherein the methylation of the SOCS-3 promoter occurs within the region from -1005 to -983 or from -754 to -737 of SEQ ID NO:3.

Wikman et al teach that using cDNA hybridization array (p.5810), SOCS-3 is shown to be down-regulated in adenoma lung cancer tissue samples as compared to normal human lung (p.5809, first column, item under "Down-regulated genes").

SOCS-3 taught by Wikman is the same as the claimed SOSC-3 of SEQ ID NO:1, encoding SEQ ID NO:2 of the claimed invention, as evidenced by WO2004022778-A1. WO2004022778-A1 teaches human SOCS-3 encoding SEQ ID NO:73, which is 100% similar to SEQ ID NO:1 as shown by MPSRCH search result, 2009, us-10-570-916.1.rng, result 2.

Although the reference does not explicitly teach that the lung cancer has a methylation of a SOCS-3 promoter, wherein the methylation of the SOCS-3 promoter occurs within the region from -1005 to -983 or from -754 to -737 of SEQ ID NO:3, however, the claimed lung cancer appears to be the same as the prior art lung cancer. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior

art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3, 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wikman et al, Oncogene, August 2002, 21: 5804-5813, and as evidenced by WO2004022778-A1 (Sutherland et al, published on 03/18/2004).

Claims 3, 29-30 are as follows;

Claim 3. (Original) The method of claim 1, wherein the step of determining the level of the transcript comprises an amplification reaction.

Claim 29. (Previously Presented) The method of claim 3, wherein the amplification reaction is selected from the group consisting of polymerase chain reaction, quantitative polymerase chain reaction, ligase chain reaction, transcription amplification, self- sustained sequence replication, dot polymerase chain reaction, and linker adapter polymerase chain reaction.

Claim 30. (Previously Presented) The method of claim 3, wherein the amplification reaction comprises SEQ ID NO:9 and SEQ ID NO: 10.

The teaching of Wikman et al has been set forth above. Wikman et al also teach the uses of PCR to confirm the gene expression differences of 10 genes detected by cDNA array, and that PCR is a more sensitive method (p.5807, first column, paragraph before last).

Wikman et al do not teach that the expression of SOCS-3 is also tested with PCR.

It would have been prima facia obvious to one of skill in the art at the time the invention was made to replace cDNA array with PCR for detecting the SOSC-3 of SEQ ID NO:1 in lung cancer, because PCR is a more sensitive method, as taught by Wikman et al.

Further, one would have expected that PCR of the SOSC-3 of SEQ ID NO: 1 would comprise SEQ ID NO:9 and SEQ ID NO: 10, because they are fragments of SEQ ID NO:1. Moreover, PCR is common in the art, and it is within the level of ordinary skill in the art to design primers for a known nucleic acid sequence.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
July 28, 2009
/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643

MPSRCH search result, 2009, us-10-570-916.1.rng, result 2

```
ESULT 2
ADL26819
ID   ADL26819 standard; cDNA; 850 BP.
XX
AC   ADL26819;
XX
DT   03-JUN-2004  (first entry)
XX
DE   Human SOCS3 encoding cDNA SEQ ID NO:73.
XX
KW   ovarian cancer; ovarian cancer-associated transcript; cytostatic;
KW   gene therapy; human; SOCS3; chromosome 17; gene; ss.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   CDS             107. .784
FT                   /*tag=  a
FT                   /product= "SOCS3"
XX
PN   WO2004022778-A1.
XX
PD   18-MAR-2004.
XX
PF   05-SEP-2003; 2003WO-AU001166.
XX
PR   05-SEP-2002; 2002AU-00951346.
XX
PA   (GARV-) GARVAN INST MEDICAL RES.
XX
PI   Sutherland R,  Henshall S,  O'brien P;
XX
DR   WPI; 2004-315574/29.
DR   P-PSDB; ADL26820.
XX
PT   Use of genes and proteins for diagnosing ovarian cancer and/or a
PT   likelihood for survival or recurrence of the disease.
XX
PS   Claim 2; SEQ ID NO 73; 447pp; English.
XX
CC   The present invention describes a method for the use of genes and
CC   proteins for diagnosing ovarian cancer and/or a likelihood for survival
CC   or recurrence of the disease, where the expression of genes and proteins
CC   is up-regulated and down-regulated or associated with the occurrence or
CC   recurrence of a specific cancer sub-type. Also described: (1) detecting
CC   an ovarian cancer-associated transcript in a biological sample; (2)
CC   diagnosing an ovarian cancer in a human or animal subject being tested;
CC   (3) detecting an ovarian cancer-associated polypeptide in a biological
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CC   sample; (4) monitoring the efficacy of a therapeutic treatment of ovarian
CC   cancer; (5) determining the likelihood of survival of a subject suffering
CC   from an ovarian cancer; and (6) an assay device for use in the diagnosis
CC   or prognosis of ovarian cancer comprising polynucleotides or antibodies
CC   immobilised to a solid phase, where each of the polynucleotides consists
CC   of a gene given in the specification and each of the antibodies binds to
CC   a polypeptide also given in the specification; and identifying a
CC   candidate compound for the treatment of ovarian cancer. An ovarian cancer
CC   -associated sequence has cytostatic activity, and can be used in gene
CC   therapy. An ovarian cancer-associated polynucleotide, vector, polypeptide
CC   or antibody can be used for the diagnosis or prognosis of ovarian cancer
CC   or for the preparation of a medicament for the treatment of ovarian
CC   cancer. The ovarian cancer that is diagnosed is an epithelial ovarian
CC   cancer selected from serous ovarian cancer, non-invasive ovarian cancer,
CC   mixed phenotype ovarian cancer, mucinous ovarian cancer, endometrial
CC   ovarian cancer, clear cell ovarian cancer, papillary serous ovarian
CC   cancer, Brenner cell or undifferentiated adenocarcinoma. The present
CC   sequence encodes human SOCS3, which is located on chromosome 17 and is
CC   used in the exemplification of the present invention.
XX
SQ   Sequence 850 BP; 148 A; 316 C; 249 G; 137 T; 0 U; 0 Other;

  Query Match             100.0%;  Score 850;  DB 2;  Length 850;
  Best Local Similarity   100.0%;  Pred. No. 7.5e-165;
  Matches  850;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 GCGCCTTCCTCTCCGCAGCCCCCCGGGATGCGGTAGCGGCCGCTGTGCGGAGGCCGCGAA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 GCGCCTTCCTCTCCGCAGCCCCCCGGGATGCGGTAGCGGCCGCTGTGCGGAGGCCGCGAA 60

Qy         61 GCAGCTGCAGCCGCCGCCGCGCAGATCCACGCTGGCTCCGTGCGCCATGGTCACCCACAG 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GCAGCTGCAGCCGCCGCCGCGCAGATCCACGCTGGCTCCGTGCGCCATGGTCACCCACAG 120

Qy        121 CAAGTTTCCCGCCGCCGGGATGAGCCGCCCCCTGGACACCAGCCTGCGCCTCAAGACCTT 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 CAAGTTTCCCGCCGCCGGGATGAGCCGCCCCCTGGACACCAGCCTGCGCCTCAAGACCTT 180

Qy        181 CAGCTCCAAGAGCGAGTACCAGCTGGTGGTGAACGCAGTGCGCAAGCTGCAGGAGAGCGG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 CAGCTCCAAGAGCGAGTACCAGCTGGTGGTGAACGCAGTGCGCAAGCTGCAGGAGAGCGG 240

Qy        241 CTTCTACTGGAGCGCAGTGACCGGCGGCGAGGCGAACCTGCTGCTCAGTGCCGAGCCCGC 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 CTTCTACTGGAGCGCAGTGACCGGCGGCGAGGCGAACCTGCTGCTCAGTGCCGAGCCCGC 300

Qy        301 CGGCACCTTTCTGATCCGCGACAGCTCGGACCAGCGCCACTTCTTCACGCTCAGCGTCAA 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 CGGCACCTTTCTGATCCGCGACAGCTCGGACCAGCGCCACTTCTTCACGCTCAGCGTCAA 360

Qy        361 GACCCAGTCTGGGACCAAGAACCTGCGCATCCAGTGTGAGGGGGGCAGCTTCTCTCTGCA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 GACCCAGTCTGGGACCAAGAACCTGCGCATCCAGTGTGAGGGGGGCAGCTTCTCTCTGCA 420

Qy        421 GAGCGATCCCCGGAGCACGCAGCCCGTGCCCCGCTTCGACTGCGTGCTCAAGCTGGTGTA 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 GAGCGATCCCCGGAGCACGCAGCCCGTGCCCCGCTTCGACTGCGTGCTCAAGCTGGTGTA 480

Qy        481 CCACTACATGCCGCCCCCTGGAGCCCCCTCCTTCCCCTCGCCACCTACTGAACCCTCCTC 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 CCACTACATGCCGCCCCCTGGAGCCCCCTCCTTCCCCTCGCCACCTACTGAACCCTCCTC 540

Qy        541 CGAGGTGCCCGAGCAGCCGTCTGCCCAGCCACTCCCTGGGAGTCCCCCCAGAAGAGCCTA 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 CGAGGTGCCCGAGCAGCCGTCTGCCCAGCCACTCCCTGGGAGTCCCCCCAGAAGAGCCTA 600

Qy        601 TTACATCTACTCCGGGGGCGAGAAGATCCCCCTGGTGTTGAGCCGGCCCCTCTCCTCCAA 660
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Db        601 TTACATCTACTCCGGGGGGCGAGAAGATCCCCCTGGTGTTGAGCCGGCCCCTCTCCTCCAA 660

Qy        661 CGTGGCCACTCTTCAGCATCTCTGTCGGAAGACCGTCAACGGCCACCTGGACTCCTATGA 720
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 CGTGGCCACTCTTCAGCATCTCTGTCGGAAGACCGTCAACGGCCACCTGGACTCCTATGA 720

Qy        721 GAAAGTCACCCAGCTGCCGGGGCCCATTCGGGAGTTCCTGGACCAGTACGATGCCCCGCT 780
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GAAAGTCACCCAGCTGCCGGGGCCCATTCGGGAGTTCCTGGACCAGTACGATGCCCCGCT 780

Qy        781 TTAAGGGGTAAAGGGCGCAAAGGGCATGGGTCGGGAGAGGGGACGCAGGCCCCTCTCCTC 840
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 TTAAGGGGTAAAGGGCGCAAAGGGCATGGGTCGGGAGAGGGGACGCAGGCCCCTCTCCTC 840

Qy        841 CGTGGCACAT 850
                ||||||||||
Db        841 CGTGGCACAT 850
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